

10/056,478

(FILE 'HOME' ENTERED AT 14:11:22 ON 24 AUG 2004)

FILE 'REGISTRY' ENTERED AT 14:12:06 ON 24 AUG 2004

E 6-MNA/CN

E ?MNA/CN

E MNA/CN

L1 3 S E3

FILE 'CAPLUS, EMBASE, BIOSIS, MEDLINE, WPIDS' ENTERED AT 14:14:06 ON 24 AUG 2004

L2 128 S 6-MNA

FILE 'REGISTRY' ENTERED AT 14:15:09 ON 24 AUG 2004

E 6-METHOXY-2-NAPHTHYLACETIC ACID/CN

L3 3 S E3-E5

E OXYCODONE/CN

L4 2 S E2-E3

FILE 'CAPLUS, EMBASE, BIOSIS, MEDLINE, WPIDS, CAOLD, USPAT2, USPATFULL, BIOTECHNO, BIOBUSINESS' ENTERED AT 14:17:56 ON 24 AUG 2004

L5 9 S L3 AND L4

L6 34 S 6-MNA AND L4

L7 26 S L6 NOT L5

FILE 'CAPLUS, EMBASE, BIOSIS, MEDLINE, WPIDS, CAOLD' ENTERED AT 14:20:50 ON 24 AUG 2004

L8 333 S L3 OR 6-MNA

L9 64 S L8 AND IBUPROFEN?

L10 31 S L9 AND (CYCLOXYGEN? OR COX?)

L11 22 DUP REM L10 (9 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 14:24:13 ON 24 AUG 2004

FILE 'CAPLUS, EMBASE, BIOSIS, MEDLINE, WPIDS' ENTERED AT 14:25:38 ON 24 AUG 2004

L12 332 S L3 OR 6-MNA

L13 129 S L12 AND (ASPIRIN? OR IBUPROFEN? OR NSAID?)

L14 44 S L13 AND (GASTROINTEST? OR GI)

L15 28 DUP REM L14 (16 DUPLICATES REMOVED)

L16 1169 S (BURCH, R? OR BURCH R?)/AU,IN

L17 226 S (GOLDENHEIM, P? OR GOLDENHEIM P?)/AU,IN

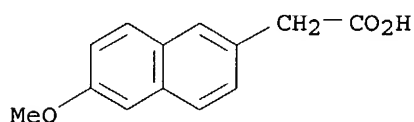
L18 107 S (SACKLER, R? OR SACKLER R?)/AU,IN

L19 1449 S L16 OR L17 OR L18

L20 2 S L19 AND (L2 OR 6-MNA)

=>

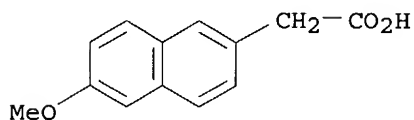
L3 ANSWER 1 OF 3 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 141969-30-4 REGISTRY
 CN 2-Naphthaleneacetic acid, 6-methoxy-, potassium salt (9CI) (CA INDEX NAME)
 OTHER NAMES:
 CN **6-Methoxy-2-naphthylacetic acid potassium salt**
 MF C13 H12 O3 . K
 SR CA
 LC STN Files: CA, CAPLUS
 DT.CA CAPLUS document type: Patent
 RL.P Roles from patents: BIOL (Biological study)
 CRN (23981-47-7)



● K

1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 2 OF 3 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 141969-29-1 REGISTRY
 CN 2-Naphthaleneacetic acid, 6-methoxy-, sodium salt (9CI) (CA INDEX NAME)
 OTHER NAMES:
 CN **6-Methoxy-2-naphthylacetic acid sodium salt**
 MF C13 H12 O3 . Na
 SR CA
 LC STN Files: CA, CAPLUS
 DT.CA CAPLUS document type: Patent
 RL.P Roles from patents: BIOL (Biological study)
 CRN (23981-47-7)

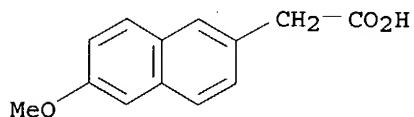


● Na

1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 23981-47-7 REGISTRY
 CN 2-Naphthaleneacetic acid, 6-methoxy- (7CI, 8CI, 9CI) (CA INDEX NAME)
 OTHER NAMES:
 CN 2-(6-Methoxy-2-naphthyl)acetic acid
 CN 6-Methoxy-2-naphthaleneacetic acid
 CN **6-Methoxy-2-naphthylacetic acid**
 CN BRL 10720

FS 3D CONCORD
 MF C13 H12 O3
 CI COM
 LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO,
 CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX,
 CHEMLIST, CSCHM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA,
 MEDLINE, PS, RTECS*, TOXCENTER, USPAT2, USPATFULL
 (*File contains numerically searchable property data)
 Other Sources: EINECS**
 (**Enter CHEMLIST File for up-to-date regulatory information)
 DT.CA Caplus document type: Conference; Dissertation; Journal; Patent
 RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study);
 FORM (Formation, nonpreparative); PREP (Preparation); PROC (Process);
 RACT (Reactant or reagent); USES (Uses)
 RLD.P Roles for non-specific derivatives from patents: BIOL (Biological
 study); PREP (Preparation); PROC (Process); USES (Uses)
 RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological
 study); FORM (Formation, nonpreparative); PREP (Preparation); PROC
 (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses);
 NORL (No role in record)
 RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological
 study); PRP (Properties); USES (Uses)



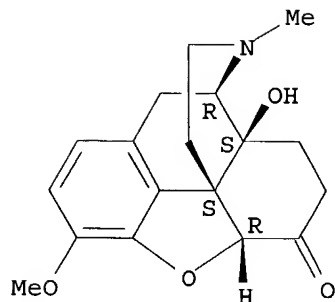
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

130 REFERENCES IN FILE CA (1907 TO DATE)
 3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 130 REFERENCES IN FILE CAPLUS (1907 TO DATE)
 1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=>

L4 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 124-90-3 REGISTRY
 CN Morphinan-6-one, 4,5-epoxy-14-hydroxy-3-methoxy-17-methyl-, hydrochloride,
 (5 α)- (9CI) (CA INDEX NAME)
 OTHER CA INDEX NAMES:
 CN Codeinone, 7,8-dihydro-14-hydroxy-, hydrochloride (6CI, 7CI)
 CN Morphinan-6-one, 4,5 α -epoxy-14-hydroxy-3-methoxy-17-methyl-,
 hydrochloride (8CI)
 OTHER NAMES:
 CN 14-Hydroxydihydrocodeinone hydrochloride
 CN 4,5 α -Epoxy-14-hydroxy-3-methoxy-N-methyl-6-oxomorphinan
 hydrochloride
 CN Dihydro-14-hydroxycodeinone hydrochloride
 CN Dihydrone hydrochloride
 CN Dihydrooxycodeinone hydrochloride
 CN Dinarkon
 CN Endone
 CN Eubine
 CN Eucodal
 CN Eukodal
 CN Eutagen
 CN Oxikon
 CN Oxycod
 CN **Oxycodon hydrochloride**
 CN Oxycodone hydrochloride
 CN Oxycon
 CN OxyContin
 CN Oxygesic
 CN Oxykodal
 CN Oxykon
 CN Pancodine
 CN Roxicodone
 CN Stupenone
 CN Supeudol
 CN Tecodin
 CN Tecodine
 CN Tekodin
 CN Thecodin
 CN Thecodine
 CN Thekodin
 FS STEREOSEARCH
 DR 13699-57-5, 30777-15-2
 MF C18 H21 N O4 . Cl H
 CI COM
 LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BEILSTEIN*, BIOBUSINESS,
 BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CBNB, CHEMCATS, CHEMLIST, CIN,
 CSCHEM, DIOGENES, EMBASE, HSDB*, IPA, MRCK*, MSDS-OHS, PIRA, PROMT,
 PROUSDDR, PS, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL
 (*File contains numerically searchable property data)
 Other Sources: EINECS**
 (**Enter CHEMLIST File for up-to-date regulatory information)
 DT.CA Caplus document type: Conference; Journal; Patent
 RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study);
 PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or
 reagent); USES (Uses); NORL (No role in record)
 RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological
 study); PREP (Preparation); PROC (Process); PRP (Properties); RACT
 (Reactant or reagent); USES (Uses); NORL (No role in record)
 CRN (76-42-6)

Absolute stereochemistry.



● HCl

314 REFERENCES IN FILE CA (1907 TO DATE)
 315 REFERENCES IN FILE CAPLUS (1907 TO DATE)
 18 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L4 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN

RN 76-42-6 REGISTRY

CN Morphinan-6-one, 4,5-epoxy-14-hydroxy-3-methoxy-17-methyl-, (5 α)-
 (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Codeinone, 7,8-dihydro-14-hydroxy- (6CI, 7CI)

CN Morphinan-6-one, 4,5 α -epoxy-14-hydroxy-3-methoxy-17-methyl- (8CI)

OTHER NAMES:

CN (-)-Oxycodone

CN 14-Hydroxydihydrocodeinone

CN 3-O-(Methyl)oxymorphone

CN 6-Oxo-14-hydroxy-7,8-dihydrocodeine

CN 7,8-Dihydro-14-hydroxycodeinone

CN Dihydro-14-hydroxycodeinone

CN Dihydrohydroxycodeinone

CN Dihydrone

CN NSC 19043

CN Oxanest

CN Oxicon

CN Oxycodone

CN **Oxycodone**

CN Oxymorphone 3-methyl ether

FS STEREOSEARCH

MF C18 H21 N O4

CI COM

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*,
 BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT,
 CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHM, DDFU,
 DIOGENES, DRUGU, EMBASE, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA,
 MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PHAR, PROMT, PROUSDDR,
 PS, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL
 (*File contains numerically searchable property data)

Other Sources: EINECS**, WHO

(**Enter CHEMLIST File for up-to-date regulatory information)

DT.CA Caplus document type: Conference; Journal; Patent

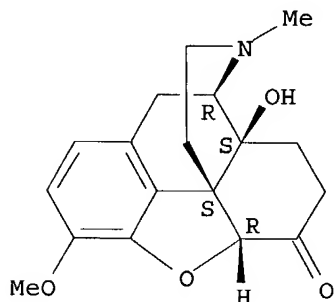
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study);
 FORM (Formation, nonpreparative); MSC (Miscellaneous); PREP
 (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or
 reagent); USES (Uses); NORL (No role in record)

RLD.P Roles for non-specific derivatives from patents: BIOL (Biological
 study); PREP (Preparation); USES (Uses)

RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological

study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

747 REFERENCES IN FILE CA (1907 TO DATE)
15 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
752 REFERENCES IN FILE CAPLUS (1907 TO DATE)
32 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=>

L11 ~~ANSWER 17 OF 22~~ CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4

AN 1997:32962 CAPLUS

DN 126:99032

TI Nonsteroidal antiinflammatory drugs and uncoupling of mitochondrial oxidative phosphorylation

AU Mahmud, Taher; Rafi, Sue S.; Scott, David L.; Wrigglesworth, John M.; Bjarnason, Ingvar

CS Academic and Clinical Rheumatology, King's College Hospital, London, SE22 8PT, UK

SO Arthritis & Rheumatism (1996), 39(12), 1998-2003

CODEN: ARHEAW; ISSN: 0004-3591

PB Lippincott-Raven

DT Journal

LA English

AB There is a lack of correlation between cyclooxygenase (COX) inhibition and nonsteroidal antiinflammatory drug (NSAID)-induced gastrointestinal (GI) damage; it has been suggested that mucosal damage may be initiated by a "topical" action of NSAIDs involving mitochondrial injury. We evaluated the effect of a range of NSAIDs and related compds. on mitochondrial function and assessed the differences between them in relation to their physicochem. properties. Stimulation of respiration, as an indicator of mitochondrial uncoupling, was measured in isolated coupled rat liver mitochondrial preps., using an oxygen electrode. Conventional NSAIDs and acidic prodrugs all had stimulatory effects on mitochondrial respiration at micromolar concns. (0.02-2.7 μ M); higher concns. were inhibitory. The uncoupling potency was inversely correlated with drug pKa ($r = -0.87$). Drugs known to have good GI tolerability, including modified flurbiprofen (dimeroflurbiprofen and nitrobutylflurbiprofen), nabumetone (a non-acidic prodrug), and non-acidic highly selective COX-2 inhibitors, did not cause uncoupling. The ability to uncouple mitochondrial oxidative phosphorylation is a common characteristic of antiinflammatory agents with an ionizable group. Modification or absence of an ionizable moiety reduces the effect on mitochondria and could lead to improved NSAID GI safety.

RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 18 OF 22 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

AN 96327479 EMBASE

DN 1996327479

TI The clinical implications of inhibition of the inducible form of cyclo-oxygenase.

AU Richardson C.; Emery P.

CS Dept. of Rheumatology Rehabilitation, University of Leeds, 36 Clarendon Road, Leeds LS2 9NZ, United Kingdom

SO Drug Safety, (1996) 15/4 (249-260).

ISSN: 0114-5916 CODEN: DRSAEA

CY New Zealand

DT Journal; General Review

FS 026 Immunology, Serology and Transplantation

030 Pharmacology

037 Drug Literature Index

038 Adverse Reactions Titles

048 Gastroenterology

LA English

SL English

AB There are 2 isoenzymes of cyclo-oxygenase (COX). There is a constitutive enzyme COX-1 which has a wide tissue distribution. In addition there is an inducible enzyme COX-2 which has a restricted tissue distribution. The inducible enzyme COX-2 is responsible for the generation of prostaglandins at sites of tissue inflammation and its inhibition is associated with an anti-inflammatory

action. The constitutive enzyme, COX-1 is responsible for the production of prostaglandins with multiple functions. One well known and clinically important function is the gastroprotective effect of the prostaglandins produced in the gastric mucosa. While selective COX-2 inhibition may be associated with a reduced incidence of gastric adverse effects, a concern remains that its inhibition at other locations may be associated with other adverse effects.

L11 ANSWER 19 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 5
AN 1996:333511 CAPLUS
DN 125:25851
TI Selective inhibition of human cyclooxygenase-2 by meloxicam
AU Churchill, L.; Graham, A.G.; Shih, C.-K.; Pauletti, D.; Farina, P.R.; Grob, P.M.
CS Department of Inflammatory Diseases, Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, CT, USA
SO Inflammopharmacology (1996), 4(2), 125-135
CODEN: IAOAES; ISSN: 0925-4692
PB Kluwer
DT Journal
LA English
AB Human cyclooxygenase-1 (hCOX-1) and -2 were expressed in stable transfected COS A.2 cells and in insect cells using a Sf9 baculovirus expression system. Inhibition of COX activity was examined using both whole cell and microsomal assays. Ibuprofen, naproxen, 6-MNA, diclofenac and indomethacin were selective for hCOX-1 or were equipotent inhibitors for COX-1 and COX-2. Piroxicam was equally inhibitory for both enzymes in the whole cell assay while it preferentially inhibited hCOX-2 in the microsomal assay. However, maximal inhibition of hCOX-2 by piroxicam plateaued at 60%. Nimesulide was equipotent in the whole-cell assay but was five-fold selective for hCOX-2 in the microsomal assay. Meloxicam preferentially inhibited hCOX-2 in the whole cell assay at concns. of 0.01 to 1 µmol/L but was an equipotent inhibitor of both enzymes at higher concns. In the microsomal assay, meloxicam exhibited high selectivity for hCOX-2 (75-fold). The preferential inhibition of hCOX-2 by meloxicam may explain the favorable gastrointestinal profile observed for meloxicam compared with other nonsteroidal antiinflammatory agents.

L11 ANSWER 20 OF 22 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1995:489958 BIOSIS
DN PREV199598504258
TI Selective inhibition of cyclooxygenase-2: Diaryl heterocycles vs classical NSAIDS.
AU Pinto, Donald J. [Reprint author]; Pitts, William J.; Copeland, Robert A.; Covington, Maryanne B.; Trzaskos, James; Magolda, Ronald
CS The Du Pont Merck Pharmaceutical Company, Inflammatory Disease Res., PO Box 80353, Wilmington, DE 19880-0353, USA
SO Medicinal Chemistry Research, (1995) Vol. 5, No. 5, pp. 394-398.
ISSN: 1054-2523.
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 9 Nov 1995
Last Updated on STN: 14 Dec 1995
AB This review discusses the in vitro and in vivo activities of selected anti-inflammatory diaryl heterocycles, as compared with selected classical NSAIDS. The diaryl heterocycle tiflamizole is a selective inhibitor of COX1 and shares the liabilities of classical NSAIDS while DuP697 is a selective inhibitor of COX2 and exhibits a unique biological profile.

L15 ANSWER 22 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 8

AN 1996:333511 CAPLUS

DN 125:25851

TI Selective inhibition of human cyclooxygenase-2 by meloxicam

AU Churchill, L.; Graham, A.G.; Shih, C.-K.; Pauletti, D.; Farina, P.R.; Grob, P.M.

CS Department of Inflammatory Diseases, Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, CT, USA

SO Inflammopharmacology (1996), 4(2), 125-135

CODEN: IAOAES; ISSN: 0925-4692

PB Kluwer

DT Journal

LA English

AB Human cyclooxygenase-1 (hCOX-1) and -2 were expressed in stable transfected COS A.2 cells and in insect cells using a Sf9 baculovirus expression system. Inhibition of COX activity was examined using both whole cell and microsomal assays. **Ibuprofen**, naproxen, 6-

MNA, diclofenac and indomethacin were selective for hCOX-1 or were equipotent inhibitors for COX-1 and COX-2. Piroxicam was equally inhibitory for both enzymes in the whole cell assay while it preferentially inhibited hCOX-2 in the microsomal assay. However, maximal inhibition of hCOX-2 by piroxicam plateaued at 60%. Nimesulide was equipotent in the whole-cell assay but was five-fold selective for hCOX-2 in the microsomal assay. Meloxicam preferentially inhibited hCOX-2 in the whole cell assay at concns. of 0.01 to 1 µmol/L but was an equipotent inhibitor of both enzymes at higher concns. In the microsomal assay, meloxicam exhibited high selectivity for hCOX-2 (75-fold). The preferential inhibition of hCOX-2 by meloxicam may explain the favorable **gastrointestinal** profile observed for meloxicam compared with other nonsteroidal antiinflammatory agents.

L15 ANSWER 23 OF 28 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 9

AN 1996:177634 CAPLUS

DN 124:277519

TI New insight into **NSAID**-induced gastropathy

AU Spangler, R. S.

CS Worldwide Strategic Produce Development, SmithKline Beecham Pharmaceuticals, King of Prussia, PA, USA

SO Inflammopharmacology (1995), 3(4), 347-50

CODEN: IAOAES; ISSN: 0925-4692

PB Kluwer

DT Journal; General Review

LA English

AB A review with 11 refs. The objective was to assess the impact of nabumetone's pharmacol. profile on gastric safety. Direct topical uptake of nabumetone by the gastric mucosa was assessed via autoradiog. The opportunity for nabumetone to cause indirect topical damage to the **gastrointestinal** tract was determined by examining the ability of 6-methoxy-2-naphthylacetic acid (6-MNA) to be secreted in the bile. The ability for 6-MNA to cause damage to the gastric mucosa via the systemic circulation was assessed via the preferential activity of 6-MNA on cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2). Nabumetone was shown not to exhibit direct uptake by the gastric mucosa when administered orally. 6-MNA, the active metabolite of nabumetone, was not found to undergo enterohepatic circulation. 6-MNA was found to act preferentially on COX-2. Nabumetone does not cause direct topical damage to the gastric mucosa because it is a nonacidic prodrug that will not concentrate in the gastric mucosa via "ion trapping". 6-MNA, the active metabolite of nabumetone, does not recirculate in the bile, and therefore will not cause damage to the gastric mucosa via secretion into the bile and reflux back into the stomach. Finally, 6-MNA has a low propensity to cause damage to the

gastric mucosa via the systemic circulation due to its preferential inhibition of COX-2.

L15 ANSWER 24 OF 28 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
AN 95153563 EMBASE
DN 1995153563
TI Actions and toxicity of nonsteroidal anti-inflammatory drugs.
AU Simon L.S.
CS Department of Medicine, New England Deaconess Hospital, 110 Francis
Street, Boston, MA 02215, United States
SO Current Opinion in Rheumatology, (1995) 7/3 (159-166).
ISSN: 1040-8711 CODEN: CORHES
CY United States
DT Journal; General Review
FS 030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
AB The use of nonsteroidal anti-inflammatory drugs (**NSAIDs**)
continues to grow, despite the known potential toxic risks associated with
it, probably because these drugs palliate pain and inflammation and are
relatively well tolerated. Unfortunately, **NSAID** use has not been
shown to have long-term beneficial effects on the natural history of
inflammatory diseases. Regardless, the **NSAID** market has reached
the 2.2 billion dollar mark, with 73,000,000 prescriptions written yearly
throughout the world. Although individual toxic events are relatively
rare, the large number of **NSAID** prescriptions ensures that all
the possible potential adverse events will likely be encountered by some
patients. Over the past year, interesting additions to the literature have
been made regarding the mechanisms of action as well as adverse reactions
associated with **NSAIDs**.

L15 ANSWER 25 OF 28 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
AN 94122329 EMBASE
DN 1994122329
TI Nabumetone: A clinical appraisal.
AU Helfgott S.M.
CS Brigham and Women's Hospital, 45 Francis St., Boston, MA 02115, United
States
SO Seminars in Arthritis and Rheumatism, (1994) 23/5 (341-346).
ISSN: 0049-0172 CODEN: SAHRBF
CY United States
DT Journal; General Review
FS 006 Internal Medicine
030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
AB Nonsteroidal antiinflammatory drugs (**NSAIDs**) have long been used
as therapy for arthritis patients. However, in some patients these drugs
can cause **gastrointestinal** hemorrhage, perforation, or ulcer
through direct topical effects, enterohepatic recirculation, and systemic
effects. In an effort to address this problem, new **NSAIDs** have
been developed. Nabumetone, which belongs to a new class of **NSAID**
, is a nonacidic agent that has been associated with a low incidence of
peptic ulcer. This article examines available clinical data on nabumetone,
including studies on **gastrointestinal** safety and effectiveness
in osteoarthritis and rheumatoid arthritis patients, and data that may

provide an explanation for nabumetone's low incidence of ulceration.

L15 ANSWER 26 OF 28 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN DUPLICATE 10
AN 93123898 EMBASE
DN 1993123898
TI Nabumetone: A 'nonacidic' nonsteroidal antiinflammatory drug.
AU Dahl S.L.
CS Gold IV Unit M4213, School of Medicine, University of Missouri, 2411
Holmes, Kansas City, MO 64108, United States
SO Annals of Pharmacotherapy, (1993) 27/4 (456-463).
ISSN: 1060-0280 CODEN: APhRER
CY United States
DT Journal; General Review
FS 030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English; Spanish; French
AB OBJECTIVE: To review the pharmacology, pharmacokinetic disposition, dosage recommendations, adverse effects, drug interactions, and efficacy of nabumetone in patients with selected rheumatic disorders and soft-tissue injuries. DATA SOURCES: Data from scientific literature were extracted, evaluated, and summarized for presentation. A MEDLINE search was conducted using the following indexing terms: antiinflammatory agents, nonsteroidal, nabumetone, rheumatoid arthritis (RA), and osteoarthritis (OA). Studies evaluating nabumetone reported in articles, abstracts, or proceedings involving human subjects were considered for inclusion. STUDY SELECTION: Special consideration was given to clinical studies using double-blind, randomized, parallel, controlled designs. Studies comparing the effectiveness and safety of nabumetone with placebo and other nonsteroidal antiinflammatory drugs (NSAIDs) were included. DATA EXTRACTION: Data from human studies published in the English language were evaluated. Trials were assessed according to study design, sample size, and description of outcomes. DATA SYNTHESIS: Nabumetone is a nonacidic prodrug that is metabolized to an active nonsteroidal antiinflammatory moiety, 6-methoxy-2-naphthylacetic acid (6-MNA). 6-MNA is a structural analog of naproxen. Like naproxen and other NSAIDs, 6-MNA possesses analgesic, antipyretic, and antiinflammatory activity. 6-MNA has a prolonged elimination half-life, ranging from 17 to 74 hours, which allows for once-daily dosing. The efficacy of nabumetone for treating symptoms of RA and OA has been established in controlled clinical trials. Nabumetone also has been studied in ankylosing spondylitis and soft-tissue injuries. Adverse effects associated with nabumetone are similar to those associated with other NSAIDs. Gastrointestinal reactions occur most frequently in the form of abdominal pain or indigestion, nausea, or vomiting. Central nervous system adverse effects occur less frequently, and are followed in order of occurrence by rashes. CONCLUSIONS: Nabumetone is a prodrug metabolized to an active metabolite structurally related to naproxen. Studies have demonstrated the efficacy of nabumetone, but no advantages over the many other NSAIDs now available.

L15 ANSWER 27 OF 28 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
AN 92360325 EMBASE
DN 1992360325
TI The unique pharmacologic profile of nabumetone.
AU Blower P.R.
CS SmithKline Beecham Pharmaceuticals, Coldharbour Road, Harlow, Essex CM19
5AD, United Kingdom
SO Journal of Rheumatology, (1992) 19/SUPPL. 36 (13-19).
ISSN: 0315-162X CODEN: JRHUA

CY Canada
DT Journal; Conference Article
FS 031 Arthritis and Rheumatism
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
AB Nabumetone is a novel nonsteroidal antiinflammatory drug (**NSAID**) with a unique pharmacologic profile. It is nonacidic and demonstrates minimal prostaglandin synthesis inhibition. Because it is nonacidic, nabumetone cannot dissociate in the stomach after oral administration. In contrast, acidic **NSAID** (active cyclooxygenase inhibitors) can dissociate and concentrate by 'ion trapping' in the gastric mucosa, inhibit prostaglandin synthesis and, therefore, cause topically induced erosive mucosal damage. After absorption, nabumetone is converted by first pass metabolism to the active metabolite, 6-methoxy-2-naphthylacetic acid (6MNA), an effective inhibitor of prostaglandin synthesis. 6MNA is hepatically, not renally, cleared and differs from other **NSAID** because it does not undergo enterohepatic circulation in animals or man. This is thought to contribute to its apparent lack of severe **gastrointestinal** irritancy. The pharmacologic profile of nabumetone can be summarized in terms of the very large 'therapeutic ratio' in comparison with other **NSAID**.

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